Investigating fatigue of less than 6 months' duration

Guidelines for family physicians

Marshall Godwin, MD, CCFP, FCFP Dianne Delva, MD, CCFP Katherine Miller, MD Jenny Molson, MD, CCFP
Neil Hobbs, MD, CCFP Susan MacDonald, MD, CCFP Caroline MacLeod, MD

ABSTRACT

OBJECTIVE To develop an evidence-based systematic approach to assessment of adult patients who present to family physicians complaining of fatigue of less than 6 months' duration. The guidelines present investigative options, making explicit what should be considered in all cases and what should be considered only in specific situations. They aim to provide physicians with an approach that, to the extent possible, is based on evidence so that time and cost are minimized and detection and management of the cause of the fatigue are optimized.

QUALITY OF EVIDENCE MEDLINE was searched from 1966 to 1997 using the key words "family practice" and "fatigue." Articles about chronic fatigue syndrome were excluded. Articles with level 3 evidence were found, but no randomized trials, cohort studies, or case-control studies were found. Articles looking specifically at the epidemiology, demographics, investigations, and diagnoses of patients with fatigue were chosen. Articles based on studies at referral and specialty centres were given less weight than those based on studies in family physicians' offices.

MAIN MESSAGE Adherence to these guidelines will decrease the cost of investigating the symptom of fatigue and optimize diagnosis and management. This needs to be proved in practice, however, and with research that produces level 1 and 2 evidence.

CONCLUSIONS Adults presenting with fatigue of less than 6 months' duration should be assessed for psychosocial causes and should have a focused history and physical examination to determine whether further investigations should be done. The guidelines outline investigations to be considered. The elderly require special consideration. These guidelines have group validation, but they need to be tested by more physicians in various locations and types of practices.

RÉSUMÉ

OBJECTIF Élaborer une approche systématique fondée sur des données probantes permettant d'évaluer les patients qui consultent leur médecin de famille se plaignant de souffrir de fatigue depuis moins de six mois. Les lignes directrices présentent des options d'investigation, expliquant en détail les aspects dont il faut tenir compte dans tous les cas et ceux qui ne devraient être considérés que dans des situations bien précises. Elles visent à offrir aux médecins une approche qui se fonde dans la mesure du possible sur des données probantes, afin de minimiser le temps requis et les coûts tout en optimisant la détection et la prise en charge des causes de la fatigue.

QUALITÉ DES DONNÉES Une recherche a été effectuée dans MEDLINE de 1996 à 1997 à l'aide des mots clés «pratique de médecine familiale» et «fatigue». Nous avons exclu les articles concernant le syndrome de la fatigue chronique. Nous avons trouvé des articles comportant des données probantes de niveau 3, sans toutefois pouvoir relever d'essais aléatoires, d'études de cohorte ou d'études de cas-témoins. Nous avons sélectionné les articles se penchant spécifiquement sur l'épidémiologie, la démographie, les investigations et le diagnostic des patients souffrant de fatigue. Les articles basés sur des études réalisées dans des centres d'aiguillage ou spécialisés ont reçu une pondération moins importante que ceux fondés sur des études dans des cabinets de médecins de famille.

PRINCIPAL MESSAGE Le respect de ces lignes directrices permettra de réduire les coûts de l'investigation du symptôme de la fatigue, et le diagnostic ainsi que la prise en charge en seront optimisés. Il est par ailleurs nécessaire d'en faire la preuve dans la pratique et grâce à des recherches produisant des données probantes de niveaux 1 et 2.

CONCLUSIONS Les adultes qui consultent souffrant de fatigue depuis moins de six mois devraient être évalués pour déterminer l'éventualité de causes psychosociales et devraient faire l'objet d'une anamnèse et d'un examen physique ciblés pour décider du bien-fondé d'une investigation plus approfondie. Les lignes directrices indiquent les investigations à considérer. Les personnes âgées exigent une attention particulière. Ces lignes directrices ont reçu une validation de groupe, mais elles devraient être mises à l'épreuve par un plus grand nombre de médecins dans diverses régions et différents genres de pratique.

This article has been peer reviewed.
Cet article a fait l'objet d'une évaluation externe.
Can Fam Physician 1999;45:373-379.

← FOR PRESCRIBING INFORMATION SEE PAGE 457

CME

Investigating fatigue of less than 6 months' duration

Patients often present with fatigue in family practice. A survey of patients registered with general practitioners in Britain[1] found 18% of people complained of fatigue; other studies report frequencies of 6.9% (Texas[2]), 13.6% (Canada[3]), and 32% (Israel[4]).

Women are three to four times more likely to complain of fatigue than men.[1,5,6] Fatigue as a presenting symptom peaks between 20 and 40 years old, declines from 40 to 75, and then increases slightly again after age 75.[6,7]

The literature overwhelmingly suggests that patients presenting with fatigue are likely to have associated psychological conditions, primarily depression, anxiety, or life stresses.[1-15] From 30% to 70% of patients complaining of fatigue have associated psychological complaints or diagnoses; physical and psychological conditions often combine to explain the fatigue. The frequency with which fatigue is related to physical problems is an important consideration in attempting to develop guidelines for investigating patients presenting with fatigue. Although the association is present regardless of the duration of the fatigue, psychosocial conditions are more likely to be a factor the longer the symptom has existed.

Despite the strong association with psychosocial problems, many patients have physical explanations for their fatigue. In 1990, Kirk et al[10] followed 71 patients presenting with fatigue. The physicians determined that 37 of the 71 (52%) had physical causes for their fatigue (mostly in the cardiovascular, respiratory, and musculoskeletal systems); 8% had fatigue brought on by medications; and 4% were fatigued due to anemia.

Morrison[7] reviewed 176 charts with diagnosis of fatigue in a family practice: 69 (39%) had physical explanations for the fatigue, 72 (41%) had psychological explanations, 21 (12%) had combined physical and psychological factors, and the remaining 14 (8%) had no discernible explanations on the chart. The psychological diagnoses were depression, anxiety, stress, adjustment reaction, and alcoholism. The main physical explanation was a viral syndrome (27 of 69); this did not include mononucleosis, which was diagnosed in a further nine patients. Various chronic diseases were thought to explain many of the symptoms—asthma, hypothyroidism, hepatitis, ischemic heart disease, diabetes, and anemia.

Sugarman and Berg[6] reviewed 118 charts of family practice patients with fatigue to determine what laboratory investigations were ordered for these patients and whether test results contributed to diagnosis. The most common investigations (75%) were complete blood count, urinalysis, erythrocyte sedimentation rate, serum chemistries, and thyroid function tests. Although 12% of test results were abnormal, they were important in confirming the diagnosis in only nine of the 118 patients.

In a similar study in Britain, Ridsdale et al[5] determined that, while 33% of the patients had at least one abnormal result from a laboratory investigation, only 19 of the 210 patients had abnormalities that were judged to be clinically important. Clinical diagnoses based on these tests were anemia (eight patients) hypothyroidism (three), infection (three), mononucleosis (three), diabetes (one), and carcinomatosis (one).

Except for suspected chronic fatigue syndrome (CFS),[16] no guidelines have been published on an approach to investigating patients presenting to family physicians with fatigue. Given the frequency with which the problem occurs in family practice, this seems unusual; however, it might be explained by the lack of strong evidence available. We thought that, despite the lack of research in the area, an attempt should be made to review the evidence that is available and provide some guidance for clinicians confronted with a problem that is often frustrating and that might lead them to do unnecessary investigations.

Process

The Family Practice Guidelines Development Group in Kingston, Ont, is an e-mail–based group of family physicians formed for the purpose of developing guidelines for family physicians by family physicians. The group focuses on problems that are common and important to family practitioners. Their goal is to produce practical guidelines that can be easily applied in clinical settings, that are evidence-based as far as evidence is available, and that reflect the experience and expertise of the family physicians in the group.

The group meets by e-mail to discuss issues in family medicine for which guidelines appear to be needed. The group had 14 members, including academic family physicians, community-based family

Drs Godwin and Delva *are Associate Professors, and* **Drs Hobbs** *and* **MacDonald** *are Assistant Professors, in the Department of Family Medicine at Queen's University in Kingston, Ont.* **Drs MacLeod** *and* **Miller** *were first-year family medicine residents at Queen's University when this article was written.* **Dr Molson** *is a family practitioner in Kingston.*

physicians, and family medicine residents, when the guideline for fatigue was developed. The group functions in the following way.

- All communication is by e-mail.
- Members suggest topics for possible guideline development and these are discussed.
- A topic is chosen for further exploration based on perceived need and importance to family practitioners.
- At least two members are chosen to do a MEDLINE or other appropriate search on the topic.
- These members report the results of the search to the group and, after further discussion, a draft guideline is produced and circulated to the group.
- Discussion, redrafting, and circulation continue until the group comes to a consensus on the format and content of the guideline.

This process was used to develop the guideline on fatigue.

Because there was no persuasive evidence to include or exclude many of the investigations, the group tried to strike a balance between including investigations for conditions that might be associated with a presenting complaint of fatigue and trying to prevent overinvestigation of conditions that are generally associated with psychosocial problems in patients' lives and not related to physical disease.

The group considered various ways of presenting the guidelines. They thought clinical assessment should be placed first, because through it a patient could be categorized as low or high risk for having a physical cause for fatigue. Clinical assessment of patients can guide decisions on which investigations should be done. Each investigation is recommended as appropriate either for all cases of fatigue or for only specific situations.

MEDLINE was searched from 1966 to 1997 using "fatigue" as a MeSH heading and as a text word and "family practice" as a MeSH heading and as a text phrase. Eighty articles were indexed under both fatigue and family practice. When articles pertaining specifically to CFS were removed, 67 remained. Limiting the list to English-language articles left 52. The titles and abstracts of these articles were reviewed to choose the articles that actually dealt with patients complaining of fatigue who presented to family doctors. Twelve articles were chosen and, from the references listed in these articles, three more articles were found for a total of 15.

Considering the frequency with which patients present to family doctors with fatigue, this would seem a small number of articles. There were, however, a larger number of articles on CFS. Articles not primarily about fatigue, but which mentioned fatigue as a side effect of medications or as a symptom in various chronic illnesses, were also more numerous.

Factors to consider

Table 1[1-15] presents our guidelines for investigating patients who present with fatigue of less than 6 months' duration. These guidelines are not intended for patients with CFS. If a patient presenting with fatigue has had the symptom for 6 months or longer, physicians should consider the possibility of CFS and determine whether the patient meets the criteria for that diagnosis. Diagnostic criteria for CFS are given in the sidebar.[17-22]

Given the frequent association between fatigue and psychosocial problems, evaluation of patients with fatigue should include a clinical review aimed at eliciting evidence of depression or other psychiatric condition. It is also important to review patients' life circumstances to determine whether patients are currently under heavy stress from changes in work, home, or relationships; the level of financial stresses; whether patients are grieving a recent loss; and whether a history of abuse or trauma could be a factor.

The greater likelihood of a psychosocial origin than a biomedical origin for patients' fatigue cannot be ignored when planning a strategy for investigation. It is important, however, to elicit patients' diagnostic beliefs because patients often believe they are suffering from an organic medical disorder (eg, viral or immunologic) and, therefore, resist psychiatric labeling or even questions that probe into that realm. Establishing and maintaining rapport, having a flexible approach, and demonstrating personal concern for patients are essential.

Studies of the cost-effectiveness of investigations of patients with fatigue have not shown the investigations to be of great value if simply performed on all patients presenting with that symptom. The choice of investigations must be guided by clinical assessment of the patient. Our recommendations are based on evidence where it is available and on the consensus of the group where evidence is not available. These guidelines are meant for adults (18 years and older) because we found no literature on children presenting with fatigue and because it was the group consensus

Table 1. Guidelines for investigating adult patients with fatigue of less than 6 months' duration

INVESTIGATION	ALWAYS PERFORM?	PERFORM ONLY IN THESE SITUATIONS
Appropriate assessment for presence of anxiety or depression[1-15]	Yes	
Appropriate assessment of current life stresses and past trauma and abuse[1-15]	Yes	
Focused history and physical examination[1-15] with special emphasis on medications,[10] existing chronic illnesses,[7,9,10] and presence of infection,[7] particularly viral	Yes (to determine whether laboratory investigations are necessary)	
Hemoglobin test[4,7,10]	No	• Presence of pallor, tachycardia, dyspnea, or other symptom suggesting anemia • Dietary or family history suggesting risk of anemia • Patient older than 65*
White blood cell count[4,7]	No	• Fever or other evidence of infection • Weight loss, lymphadenopathy • Patient older than 65*
Erythrocyte sedimentation rate[6†]	No	• Evidence of inflammatory arthritis • Concern about occult malignancy • Patient older than 65*
Electrolyte assessment[5,6]	No	• Patient taking medication known to affect electrolyte balance (eg, diuretics, steroids) • Indication of a medical condition causing electrolyte imbalance (Cushing's disease, Addison's disease, parathyroidism)
Renal function tests† (urea and creatinine levels and urinalysis)	No	• Patient taking medication known to affect renal function • Symptoms or signs possibly associated with renal disease (elevated blood pressure, edema, generalized pruritus
Glucose test[5,7,10] (urinalysis only for investigating polydipsia and polyurea)	No	• History of gestational diabetes (women) • Known diagnosis of diabetes mellitus • Symptoms of polydipsia and polyurea • Unexplained peripheral neuropathy • Patient older than 65*
Thyroid-stimulating hormone test[5,7]	No	• Presence of goitre • History of thyroiditis • Symptoms and signs suggesting hypothyroidism (dry hair and skin, change in bowel habit, change in menses) • Patient older than 65*
Chest x-ray examination†	No	• Smoker with cough or hemoptysis (especially if older than 50) • History of exposure to asbestos or other pulmonary occupational hazard • Exposure to tuberculosis
Other investigations†	No	• As indicated by history and physical examination findings • Weight loss and changes in bowel habits should prompt gastrointestinal investigations*

**The elderly are not well represented in the literature. The group's consensus, after consultation with experts in care of the elderly, is that they are more likely to have physical causes of fatigue, especially if the symptom is new. We recommend lowering the threshold for investigation for this group.*

†Recommended by group consensus only; no evidence available in the literature.

that fatigue is an unusual presentation for a child. While fatigue in children could be due to psychosocial causes (especially school or home disturbances), it should probably be investigated more rigorously than we recommend for adults. Also, we treated the elderly as a special case when we made recommendations for some investigations.

Strength of evidence

The research on diagnostic interventions for patients presenting with fatigue is not strong; no randomized trials, no cohort studies, and no case-control studies were found. All the studies we found were descriptive; most were retrospective. Therefore, we had to base these guidelines on level 3 evidence (descriptive studies and expert opinion). Readers should keep this in mind when making clinical decisions based on the guidelines, and family medicine researchers should note the paucity of evidence in this area and perhaps take steps to address the problem.

Benefits, harms, and costs

If too liberal, guidelines can lead to overinvestigation, increased patient anxiety, and elevated health care costs. If too conservative, guidelines can lead to missed diagnoses, illness, and litigation. This cost-benefit assessment should be considered for any guideline. We had no persuasive evidence on which to base our decisions, but the evidence and experience available strongly suggested that most adult patients presenting with fatigue of short duration do not have serious physical causes for their symptoms, often have psychosocial issues that need to be managed, and should not routinely have multiple investigations.

Chronic fatigue syndrome

Determining whether patients presenting with fatigue meet the criteria for CFS is an important consideration. From 4% to 30% of patients who present with fatigue meet the criteria[17-22] (lower percentages indicate incidence in general populations; higher percentages incidence in referred patients). Criteria for investigating and diagnosing CFS are published in the literature[16] and are available on the Internet at **http://www.lifelines.com/cfstxt.html** and **http://www.hugme.com/med/me/cdc-cfs.html**.

Criteria for diagnosis of chronic fatigue syndrome. Clinically evaluated, unexplained, persistent or relapsing chronic fatigue is of new or definite onset (not lifelong); is not the result of ongoing exertion; is not substantially alleviated by rest; and results in substantial reduction in previous levels of occupational, educational, social, or personal activities; and the concurrence of four or more of the following symptoms, all of which must have persisted or recurred during 6 or more consecutive months of illness and must not have predated the fatigue.

- Self-reported impairment of short-term memory or concentration severe enough to cause substantial reduction in previous levels of occupational, educational, social, or personal activities
- Sore throat
- Tender cervical or axillary lymph nodes
- Muscle pain
- Multi-joint pain without joint swelling or redness
- Headaches of new type, pattern, or severity
- Unrefreshing sleep
- Postexertional malaise lasting more than 24 hours

Assessments. If patients have the length (6 months) and severity of fatigue described above, and if four of the listed criteria are met, then the condition must also meet the criteria of being "clinically evaluated and unexplained." The US Centers for Disease Control and Prevention recommend the following assessments for evaluating patients for a diagnosis of CFS.

- Full history and physical examination
- Mental status examination (abnormalities to be followed up by appropriate psychiatric, psychological, or neurologic examination)
- Complete blood count, erythrocyte sedimentation rate, alanine aminotransferase, total protein, albumin, alkaline phosphatase, calcium, phosphorus, glucose, blood urea nitrogen, electrolytes, creatinine, and thyroid-stimulating hormone tests and urinalysis
- Additional tests as clinically indicated to exclude other diagnoses.

Key points

- A group of family physicians based in Kingston, Ont, developed these guidelines based on the literature and consensus among themselves.
- Fatigue of less than 6 months' duration in adults most commonly has psychosocial causes, especially work, marital or financial stress, grieving a recent loss, or history of abuse.
- Physical causes of fatigue are less common than psychosocial causes and can usually be diagnosed by a focused history and physical examination.
- Laboratory investigations for fatigue should be used only when specific diagnoses, suggested by history and physical examination, are identified.

Validation

These guidelines have been validated only by the input and review of a group of practising physicians. For full validation, they need to be assessed in clinical settings and proved in a prospective clinical trial.

Conclusion

Fatigue is a common presenting symptom in family practice; its root is frequently psychosocial. Although physical causes are less common than psychosocial causes, it is important that patients be assessed for associated symptoms or risk factors so that appropriate investigations can be performed when indicated. The guidelines presented here attempt to provide a reasonable, and where available evidence based, approach to evaluating patients presenting with fatigue. Available evidence is only at level 3, however, and prospective evaluation of the recommendations in primary care is needed to confirm their validity.

Acknowledgment

No sponsors, financial or otherwise, supported these guidelines. They were developed by a group of practising family physicians and residents associated with the Department of Family Medicine at Queen's University in Kingston, Ont. The Family Practice Guidelines Development Group in Kingston includes the authors of this article and Drs Ian Casson, Ian Crawford, Jane Griffiths, Sen Mei Lim, Gregory Patey, Sarita Verma, and Ruth Wilson.

Correspondence to: *Dr M. Godwin, Associate Professor, Department of Family Medicine, Queen's University, PO Bag 8888, 220 Bagot St, Kingston, ON K7L 5E9*

References

1. Pawlikowska T, Chalder T, Hirsch SR, Wallace P, Wright DJ, Wessely SC. Population-based study of fatigue and psychological distress. *BMJ* 1994;308(6931):763-6.
2. Katerndahl DA. Differentiation of physical and psychological fatigue. *Fam Pract Res J* 1993;13(1):81-91.
3. Cathebras PJ, Robbins JM, Kirmayer LJ, Hayton BC. Fatigue in primary care: prevalence, psychiatric comorbidity, illness behaviour, and outcomes. *J Gen Intern Med* 1992; 7(3):276-86.
4. Shahar E, Lederer J. Asthenic symptoms in a rural family practice. Epidemiologic characteristics and a proposed classifiaction. *J Fam Pract* 1990;31(4):257-61.
5. Ridsdale L, Evans A, Jerrett W, Mandalia S, Asler K, Vora H. Patients with fatigue in general practice: a prospective study. *BMJ* 1993;307(6896):103-6.
6. Sugarman JR, Berg AO. Evaluation of fatigue in a family practice. *J Fam Pract* 1984;19(5):643-7.
7. Morrison JD. Fatigue as a presenting complaint in family practice. *J Fam Pract* 1980;10(5):795-801.
8. Rockwell DA, Burr BD. The tired patient. *J Fam Pract* 1977;5(5):853-7.
9. Lewis G, Wessely S. The epidemiology of fatigue. *J Epidemiol Community Health* 1992;46:92-7.
10. Kirk JK, Douglass R, Nelson E, Jaffe J, Lopez A, Ohler J, et al. Chief complaint of fatigue: a prospective study. *J Fam Pract* 1990;30(1):33-41.
11. Walker EA, Katon WJ, Jemelka RP. Psychiatric disorders and medical care utilization among people in the general population who report fatigue. *J Gen Intern Med* 1993; 8(8):436-40.
12. Ward MH, Delisle H, Shores JH, Slocum PC, Foresman BH. Chronic fatigue complaints in primary care: incidence and diagnostic patterns. *J Am Osteopath Assoc* 1996; 96(1):34-46.
13. Ridsdale L, Evans A, Jerrett W, Mandalia S, Osler K, Vora H. Patients who consult with tiredness: frequency of consultation, perceived causes of tiredness and its association with psychological distress. *Br J Gen Pract* 1994; 44(386):413-6.
14. Gerber PD, Barrett JA, Oxman TE, Manheimer E, Smith R, Whiting RD. The relationship of presenting physical complaints to depressive symptoms in primary care patients. *J Gen Intern Med* 1992;7(2):170-3.
15. Elnicki DM, Shockcor WT, Brick JE, Beynon D. Evaluating the complaint of fatigue in primary care: diagnoses and outcomes. *Am J Med* 1992;93(3):303-6.
16. Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Study Group. *Ann Intern Med* 1994; 121(12):953-9.

17. Lane TJ, Matthews DA, Manu P. The low yield of physical examinations and laboratory investigations of patients with chronic fatigue. *Am J Med Sci* 1990; 299(5):313-8.
18. Manu P, Lane TJ, Matthews DA. Chronic fatigue and chronic fatigue syndrome: clinical epidemiology and aetiological classification. *Ciba Found Symp* 1993;173:23-31.
19. Manu P, Matthews DA, Lane TJ. Depression among patients with a chief complaint of chronic fatigue. *J Affect Disord* 1989;17(2):165-72.
20. Manu P, Lane TJ, Matthews DA. Somatization disorder in patients with chronic fatigue. *Psychosomatics* 1989; 30(4):388-95.
21. Manu P, Matthews DA, Lane TJ. The mental health of patients with a chief complaint of chronic fatigue. A prospective evaluation and follow up. *Arch Intern Med* 1988;148(10):2213-7.
22. Manu P, Lane TJ, Matthews DA. The frequency of the chronic fatigue syndrome in patients with symptoms of persistent fatigue. *Ann Intern Med* 1988; 109(7):554-6.